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Chemical constituents of *Cardiospermum corindum* L. and their distribution in Sapindaceae

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ABSTRACT

Phytochemical investigation on the aerial parts of *Cardiospermum corindum* L. led to the isolation of two triterpenes [friedelin (**1**) and friedelinol (**2**)], two coumarins, [umbelliferone (**4**) and scopoletin (**5**)], three methoxylated flavones [umuhengerin (**3**), luteolin 3',4'-dimethyl ether (**6**) and chrysoeriol (**7**)], one non-cyanogenic glucoside [epidermin (**8**)] and one cyclitol [(*L*)-quebrachitol (**9**)]. To our knowledge, **2, 3, 6** and **8** were isolated for the first time within Sapindaceae. Of these classes of metabolites, the distribution of methoxylated flavonoids in *Cardiospermum* is reviewed, including the new records, indicating that polymethoxylated flavonoid (**3**) may be value as chemotaxonomic markers for this genus.

1. Subject and source

Cardiospermum L. is included into the Paullinieae tribe (Sapindoideae, Sapindaceae) and comprises 16 species of herbs, vines or suffrutescent herbs of pantropical distribution (Ferruci, 2000; Urdampilleta et al., 2012). Some species have important biological activities, such as anti-inflammatory, antipyretic, anti-arthritis (Sheeba and Asha, 2009), and are popularly employed in the treatment of central nervous system diseases (Kumar et al., 2011), rheumatism, and as a diuretic (Agra et al., 2008). *Cardiospermum corindum* L. was collected at the base of Pico do Jabre (7°15′34.27″ S, 37°23′8.53″ W), Paraiba, Brazil, in June 2009. The plant material was identified by Prof. Dr. Maria de Fátima Agra (UFPB). A voucher specimen (No. M.F. Agra et al. 6898) was deposited in the Herbarium Prof. Lauro Pires Xavier (JPB), at the same University.

2. Previous works

Previous phytochemical studies of *C. corindum* revealed the presence of 3′,4′-di-*O*-methyl luteolin-7-*β*-D-glucuronide (Adinarayana and Sarada, 1989; Rao et al., 1992), *myo*-inositol (Adinarayana and Sarada, 1989), 1-methyl 4-{[2-(4-nitrophenyl) ethenyl] sulfonyl}benzene, 1-{[2-methoxy-2 (4-nitrophenyl) ethyl] sulfonyl} 4-methyl-benzene (Adinarayana et al., 1987), *β*-sitosterol and stigmasterol (Adinarayana and Sarada, 1989).

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3. Present study

Air-dried and powdered *C. corindum* aerial parts (1102 g) were extracted exhaustively with 96% aqueous ethanol solution at room temperature. The combined extracts were filtered and concentrated under reduced pressure at 40 °C affording a crude extract (126.38 g). This extract was suspended in MeOH–H_2O (70:30 v/v) and successively fractionated with *n*-hexane, CH_2Cl_2 and *n*-BuOH. The CH_2Cl_2 extract (9.1 g) was subjected to CC on silica gel using step gradients of *n*-hexane-EtOAc and EtOAc-MeOH (system 1) to obtain 152 fractions combined according to their TLC profiles into 17 major fractions (Fr1-Fr17). Fraction Fr2 (0.12 g) was purified by prep. TLC (*n*-hexane-EtOAc, 95:5 v/v) to give (**1**) (90 mg). Fraction Fr3 (0.04 g) was subjected to silica gel CC using the system 1 to give a mixture of (**1**) and (**2**) (20 mg). From fraction Fr9, compound (**3**) (52 mg) was obtained as a precipitate after solvent drying. Fraction Fr10 (0.10 g) was subjected to silica gel CC using the system 1 and purified by prep. TLC (*n*-hexane-EtOAc, 60:40 v/v) to yield (**4**) (1 mg). While concentrating fraction Fr11 (0.05 g), a precipitate was formed which was then filtered under vacuum. The precipitate was refractionated by silica gel CC using the system 1 and purified by prep. TLC (*n*-hexane-EtOAc, 50:50 v/v) to give (**5**) (6.6 mg) and mixture of (**6**) and (**7**) (5.9 mg). Fraction Fr13 (0.09 g) was subjected to silica gel CC using system 1. Subfraction Fr13.1 was chromatographed in silica gel CC using gradient with $CHCl_3$–MeOH and purified by prep. TLC ($CHCl_3$–MeOH, 85:15 v/v) to yield (**8**) (12.8 mg). From fraction Fr15 obtained (**9**) (122 mg) as precipitate after solvent drying.

The structures of the isolated compounds (Fig. 1) were elucidated according to their spectroscopic data (IR, ^1H and ^{13}C NMR, one and two-dimensional techniques) and by comparison with those of literature. They were identified as friedelin (**1**) (Akihisa et al., 1992), friedelinol (**2**) (Salazar et al., 2000), umuhengerin (**3**) (Rwangabo et al., 1988), umbelliferone (**4**) (Liu and Tian, 2004), scopoletin (**5**) (Vasconcelos et al., 1998), luteolin 3′,4′-dimethyl ether (**6**) (Stevens et al., 1999), chrysoeriol (**7**) (Park et al., 2007), epidermin (**8**) (Lechtenberg et al., 1996) and (*L*)-quebrachitol,(**9**) (Huang and Luo, 1994).

4. Chemotaxonomic significance

Our phytochemical efforts on the CH_2Cl_2 extract of *Cardiospermum corindum* resulted in the isolation and identification of two triterpenes (**1, 2**), two coumarins (**4, 5**), three methoxylated flavones (**3, 6, 7**), one non-cyanogenic glucoside **(8**) and one cyclitol (**9**). This is the first report for compound **9** from *C. corindum*, compounds **1**–**6**, and **8** from a *Cardiospermum* species, and compounds **2**, **3, 6** and **8** in the Sapindaceae family (Fig. 1).

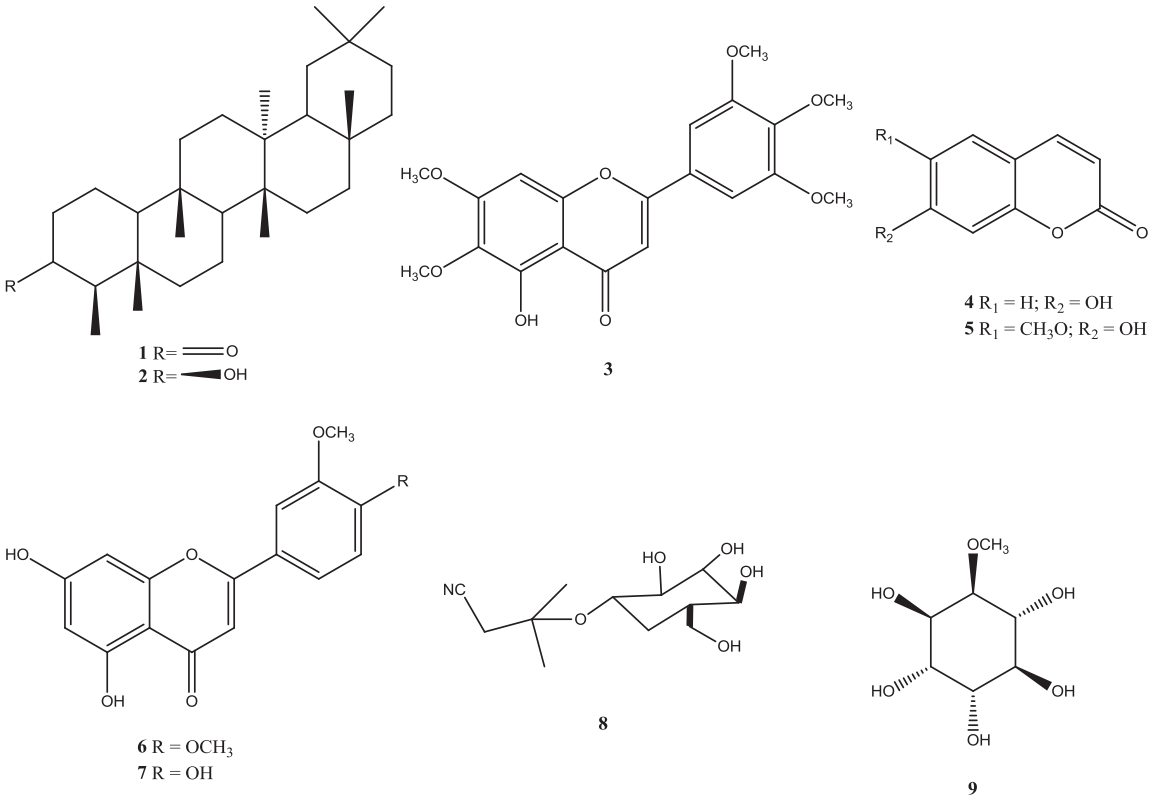

Fig. 1. Structures of compounds **1**–**9**.

Species of Sapindoideae subfamily seem to be characterized by the occurrence of triterpenes, mainly oleanane derivatives such as friedelin (Umadevi and Daniel, 1991). Coumarins have been reported in other Sapindaceae genera (Arisawa et al., 1984; Cheng et al., 2009), however the presence of **4** and **5** were only described for species of Hippocastanoideae (Sapindaceae), such as *Aesculus assamica, A. pavia* and *A. hippocastanum* (Liu et al., 2005; Paolo et al., 2007; Persson and Persson, 2010). In this study, the isolation of **9** for the first time from *C. corindum* contributes for mapping the distribution of cyclitols in Sapindaceae (Umadevi and Daniel, 1991; Vernon et al., 1993).

Non-cyanogenic glucosides, such as **8**, are found not only in plants but also in the defense secretion of caterpillars, moths and some bugs (Aldrich et al., 1990; Harborne et al., 1999). In the plant kingdom, it has been reported from *Hordeum vulgare* (Gramineae) (Pourmohseni et al., 1993) and *Rhodotypos scandens* (Rosaceae) (Lechtenberg et al., 1996).

Of the three methoxylated flavones (**3, 6, 7**) isolated from *C. corindum*, **3** and **6** are rare flavones, which have not yet been reported for Sapindaceae species. In the literature there are few reports for the isolation of hydroxylated polymethoxyflavones such as **3**, which was isolated from Rutaceae, Lamiaceae, Asteraceae and Acanthaceae (Andersen and Markham, 2006; Dong et al., 2010). Compound **6** has previously been isolated from Asteraceae, Scrophulariaceae and Hepaticae (Andersen and Markham, 2006). In Sapindaceae, only the *O*-glucuronide derivate from **6** was found in *C. corindum* and *Cardiospermum canescens* (Adinarayana and Sarada, 1989; Rao et al., 1992). Chrysoeriol (**7**) was previously isolated from *Cardiospermum halicacabum* (Wei et al., 2011; Jeyadevi et al., 2013; Cheng et al., 2013).

Only these three species of *Cardiospermum* above mentioned have been studied for their flavonoid contents. In these studies, other methoxylated flavones were also isolated, apigenin 7-methyl ether and apigenin 7,4'-dimethyl ether from *C. halicacabum* and *C. canescens* (Umadevi and Daniel, 1991), and chrysoeriol 7-*O*-glucuronide and acacetin only in *C. halicacabum* (Rao and Gunasekar, 1987; Umadevi and Daniel, 1991) Additionally, a dimethyl ether flavonol was found in *C. halicacabum*, kaempferol 3′,4′-dimethyl ether (Umadevi and Daniel, 1991).

All the compounds here described for *C. corindum* have also been found in some genera distributed in different subfamilies of Sapindaceae (Umadevi and Daniel, 1991) with the exception of the pentamethoxylated flavonoid (**3**) which has not yet been reported in this family. In this way, the search for polymethoxylated flavonoids in *Cardiospermum* and related genera should indicate if they can be used as chemotaxonomic markers for this clade.

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